



# Re-evaluating revascularization

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Editorial

This issue of *Heart and Metabolism* is dedicated to a core aspect of cardiology, revascularization. Although atherosclerosis is often viewed as a seemingly simple plumbing problem, this issue highlights the complexity of the underlying coronary physiology and the multiple pathways that can lead to myocardial ischemia. For patients with stable angina, these complexities act in concert to influence decisions regarding revascularization. To appreciate these complexities better, and to enjoy the content of this issue, it is best to read the articles in an order that differs from our stereotypical layout.

The historic journey from early physiology to present day percutaneous and surgical revascularization is beautifully told in the Refresher Corner article by Spencer King. We are privileged to have the story explained by someone so intimately involved with the evolution of revascularization. This unusual Refresher Corner uses the history of revascularization as a backdrop to the dilemmas that now face cardiologists in interpreting the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE), the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI-2D) and the Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) trials. These trials, and their impact on contemporary practice, are a theme that echoes through all the articles in this issue.

My recommendation would be to continue your journey by reading the Basic Article by Maria Siebes on coronary physiology beyond the stenosis. This article concisely and precisely introduces the complexities of the vascular and myocardial contributions to coronary artery blood flow and its distribution to the distal myocardium. The concepts are summarized and interlinked in a way that reveals the author as one of the doyennes of coronary physiology. Particularly compelling is the enormous effect that very small changes in minimal lumen diameter of a stenosis have on its resistance, and how in turn this affects the distal microvasculature due to the pressure dependence of autoregulation and hyperemic "minimal" microvascular resistance. At the end of reading this article you will be convinced that lumenography is a crude basis for decision-making. This view is greatly aided by the author introducing and explaining the current clinical and experimental physiological indices of stenosis severity and microvascular function. The concepts are very well illustrated and reinforced by the figures within this article and they provide a firm foundation to the Case Report, which I recommend as the next stop on the journey through this issue.

The Case Report by Paola Capozza and Giancarlo Todiere involves two patients with similar acute presentations with myocardial ischemia but with very different causative pathologies.

These cases serve to highlight that it is not the coronary artery but the myocardium that should be the focus/center of our attention and analyses. This shift in focus is given a Copernican paradigm with myocardial ischemia at the center of a newly appreciated solar system. Within this solar system there are numerous orbiting planets of which atherosclerotic fixed stenosis is only one of the numerous pathologies that can lead to myocardial ischemia; in isolation or, much more commonly, in concert with other pathologies affecting microvascular resistance and/or blood rheology. This shift in focus, away from atherosclerotic stenosis and towards an integrative view of the effects of varied pathologies on the myocardium, is reinforced in the Metabolic Imaging article.

Declan O'Regan and Stuart Cook are interested in the biochemical consequences of myocardial ischemia and how these can be interrogated by magnetic resonance imaging (MRI). A deficit in myocardial perfusion, whether imaged by a radionuclide, echo contrast or MRI, is often equated with ischemia. However, it is important to remember that all that is being highlighted are heterogeneities in myocardial perfusion, usually by the presence of vasodilating stressors. In contrast, the processes discussed in this article rely on physical/chemical changes in the composition of the myocardium that occur as a direct consequence of ischemia. These changes are revealed using specific MRI pulse and acquisition sequences, (T2 edema imaging) or contrast agents, (late gadolinium enhancement). The former provides a signature of the volume of myocardium that was ischemic and the latter the volume that is irreversibly injured (infarcted). Individually, these imaging modalities can be used to provide more detailed information about the etiology of chronic and acute heart disease. In combination, the authors illustrate how these imaging techniques provide a measure of myocardial salvage and can be used as surrogate endpoints in clinical trials. Detailed phenotyping of

this kind would have been useful in the cases reported by Paola Capozza and Giancarlo Todiere; however, they can also probably be used to individualize management using lessons learnt from clinical trials. Finally, this brings us to the heart of this issue – how to select patients for revascularization.

In the New Therapeutic Approaches article by Christian Seiler we are reminded through his group's seminal work that endogenous collaterals are common, but the support they provide shows considerable individual variability. Other than exercise, and perhaps enhanced external counterpulsation, there are no reliable means to enhance this support and so far trials delivering angiogenic factors have failed to bring any clinical improvement. Therefore, at present, the only viable means of revascularization is by percutaneous coronary intervention (PCI) and coronary artery bypass surgery.

The PCI and coronary artery bypass surgery trials mentioned by Spencer King are expanded on in the Main Clinical article by Mandeep Sidhu and William Boden and in Hot Topics by Alda Huqi. The Main Clinical article focusses on the COURAGE, BARI-2D and the Surgical Treatment for Ischemic Heart Failure (STITCH) trials and how their findings can be used to interpret the New York State PCI Registry and FAME 2. Similarly, Alda Huqi takes a very analytical and sideways look at the messages these trials communicate and the biases that may undermine registries and even FAME 2. The authors of both these articles come to similar, coherent and compelling conclusions. In patients with stable angina optimal medical therapy can be safely used first line and revascularization can be reserved for those that have quality of life-limiting symptoms despite maximal therapy. Old and new evidence suggests surgical revascularization is favored in patients with diabetes while  $\beta$ -blocker use can be reviewed in those patients with preserved left ventricular function who have not had an acute cardiac event in the past year. Is it really that simple? •